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EXAMINER	
JANSSEN, SHANNON L	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/537,588	PASCHKE, MATTHIAS	
	Examiner	Art Unit	
	SHANNON JANSSEN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 24-30* is/are pending in the application.

4a) Of the above claim(s) *2, 10-21 and 24-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 June 2005 and 02 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *June 6, 2005 and September 2, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-21 and 24-30 are currently pending. The amendment received June 6, 2005 canceled claims 22 and 23, amended claims 3, 6-10, and 12-19, and added claims 24-30. Claims 2, 10-21 and 24-30 have been withdrawn and claims 1 and 3-9 are currently under consideration.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-9 in the reply filed on June 22, 2009 and further clarified on July 7, 2009 is acknowledged. The traversal is on the ground(s) that the special technical feature is not two fusion proteins and the nucleic acids encoding the fusion proteins, but that the special technical feature requires the two fusion proteins to have different folding requirements and translocation sequences. This is not found persuasive because the limitations regarding folding state (e.g.: that the fusion protein is translocated in an essentially folded or unfolded state) are not given patentable weight because they are interpreted as a process of making and not the end product currently claimed (e.g.: a specific structure that would provide different folding requirements is not presently in the claims). In addition, Winter et al. (US Patent 6,291,650, issued September 18, 2001, cited in the previously mailed restriction requirement) do teach proteins fused to a phage coat protein leader (i.e.: translocation) sequence (throughout document, see particularly Example 5). Further, Weiner et al. (US Patent 6,335,178, granted January 1, 2002) teach a different translocation sequence (e.g.: a twin arginine translocation sequence; see col 1, 2, 10, and examples 1-5). It would have been obvious to one of skill in the art to utilize the alternative translocation

sequence taught by Weiner et al. to take advantage of the ability of the Tat pathway to transport folded proteins. One would have had a reasonable expectation for success because Weiner et al. teach that the translocation sequences translocate functional folded proteins through the cell membrane (see col 1, 2, 10, and col 35, para 2 - col 36, para 1).

The requirement is still deemed proper and is therefore made FINAL.

Claims 10-21 and 24-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 22, 2009 and further clarified in the response filed on July 7, 2009.

Applicant's election of the species of (a) a first fusion protein fragment: phage coat protein (claim 4) and a second fusion protein fragment: a protein encoded by a cDNA (claim 3), (b) interaction domain for a first protein: a leucine zipper domain (claim 6) and interaction domain for a second protein: a leucine zipper domain (claim 6), and (c) a translocation sequence for a first fusion protein: a Sec-dependent sequence (claim 7) and a translocation sequence for a first fusion protein: a Tat-dependent sequence (claim 8) in the reply filed on June 22, 2009 and further clarified in the response filed on July 7, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim 2 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on June 22, 2009 and further clarified in the response filed on July 7, 2009.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to German application 10256669.0, filed December 4, 2002. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. The present application also claims status as a National Stage entry of PCT/EP2003/013709, filed December 4, 2003.

Information Disclosure Statement

The information disclosure statement filed June 6, 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. A copy was not provided for the citations which are crossed out.

The information disclosure statement filed September 2, 2005 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. German patent document 19819889 does not have an English

language abstract. It has been placed in the application file, but the information referred to therein has not been considered. In addition, it fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The "K. Dane Wittrup" reference "Phage on Display" was not provided. It has been placed in the application file, but the information referred to therein has not been considered. All other references are being considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-5 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites wherein the protein or protein fragment of the first fusion protein and the protein translocation sequence is a phage coat protein. It is unclear how a phage coat protein can be a protein translocation sequence. A phage coat protein comprises a translocation sequence. Claim 5 fails to further clarify this issue and is similarly rejected.

Claim 9 recites the limitation "the protein" in line 2. There is insufficient antecedent basis for this limitation in the claim. Claim 1 (from which claim 9 depends)

recites a first fusion protein and a second fusion protein. It is unclear what protein applicant is referring to.

Invention as claimed

The present invention is drawn to a protein mixture comprising: a) at least a first fusion protein comprising: i) a protein or protein fragment, ii) an interaction domain and iii) a protein translocation sequence which effects that the fusion protein upon expression in a bacterium is translocated through the cytoplasmic membrane in an essentially unfolded state, and b) at least a second fusion protein comprising: i) a protein or protein fragment, ii) an interaction domain and iii) a protein translocation sequence which effects that the fusion protein upon expression in a bacterium is translocated through the cytoplasmic membrane in an essentially folded state, wherein the interaction domain of the first fusion protein can bind to those of the second fusion protein, and various embodiments.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-7, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Crameri et al. (Display of biologically active proteins on the surface of filamentous phages: a cDNA cloning system for selection of functional gene products linked to the genetic information responsible for their production, 1993, Gene, vol 137, pp 69-75).

Regarding present **claim 1**, Crameri et al. teach a) a first fusion protein comprising: i) PIII (i.e.: a protein or protein fragment; see p 70, col 2, para 2), ii) a Jun Leucine zipper interaction domain (see p 70, col 1, para 4, col 2, para 2), and iii) wherein PIII is the phage coat protein comprising the pelB signal sequence (i.e.: a protein translocation sequence which effects that the fusion protein upon expression in a bacterium is translocated through the cytoplasmic membrane in an essentially unfolded state; see p 70, col 1, para 4, col 2, para 2, Fig. 1), and b) a second fusion protein comprising: i) a cDNA from a cDNA library (i.e.: protein or protein fragment), ii) a Fos Leucine zipper interaction domain (see p 70, col 1, para 4, col 2, para 2,and iii) a pelB signal sequence (i.e.: a protein translocation sequence which effects that the fusion protein upon expression in a bacterium is translocated through the cytoplasmic membrane), wherein the interaction domain of the first fusion protein can bind to those of the second fusion protein (throughout document, see particularly p 70, col 1, para 4, Fig. 1). **Note:** the limitations regarding folding state (e.g.: that the fusion protein is translocated in an essentially folded or unfolded state) are not given patentable weight because they are interpreted as a process of making and not the end product currently claimed (e.g.: a specific structure that would provide different folding requirements is not presently in the claims).

Regarding present **claim 3**, Crameri et al. teach a second fusion protein comprising a cDNA from a cDNA library (see p 70, col 1, para 4, Fig. 1).

Regarding **claims 4-5**, Crameri et al. teach the M13 pIII phage coat protein (see p 70, col 2, para 2).

Regarding **claim 6**, Crameri et al. teach the first fusion protein with a Jun leucine zipper interaction domain and the second fusion protein with a Fos leucine zipper interaction domain (see p 70, col 2, para 2).

Regarding **claim 7**, Crameri et al. teach wherein the first fusion protein comprises the pelB signal sequence (i.e.: Sec-dependent signal sequence; see p 70, col 1, para 4, col 2, para 2, Fig. 1).

Regarding **claim 9**, Crameri et al. teach covalent linking of the Jun and Fos leucine zippers (i.e.: the first fusion protein is covalently bound to the second fusion protein through the leucine zippers; see p 70, col 1, para 4, Fig. 1).

Therefore, the teachings of Crameri et al. anticipate present claims 1, 3-7, and 9.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 3-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crameri et al. (Display of biologically active proteins on the surface of filamentous phages: a cDNA cloning system for selection of functional gene products linked to the genetic information responsible for their production, 1993, Gene, vol 137, pp 69-75) and Weiner et al. (US Patent 6,335,178, granted January 1, 2002), as evidenced by Wu et al. (Membrane targeting and translocation of bacterial hydrogenases, 2000, Arch Microbiol, Vol 173, pp 319-324).

Regarding present **claim 1**, Crameri et al. teach a) a first fusion protein comprising: i) PIII (i.e.: a protein or protein fragment; see p 70, col 2, para 2), ii) a Jun Leucine zipper interaction domain (see p 70, col 1, para 4, col 2, para 2), and iii) wherein PIII is the phage coat protein comprising the pelB signal sequence (i.e.: a protein translocation sequence which effects that the fusion protein upon expression in a bacterium is translocated through the cytoplasmic membrane in an essentially unfolded state; see p 70, col 1, para 4, col 2, para 2, Fig. 1), and b) a second fusion protein comprising: i) a cDNA from a cDNA library (i.e.: protein or protein fragment), ii) a Fos Leucine zipper interaction domain (see p 70, col 1, para 4, col 2, para 2,and iii) a pelB signal sequence (i.e.: a protein translocation sequence which effects that the fusion protein upon expression in a bacterium is translocated through the cytoplasmic membrane), wherein the interaction domain of the first fusion protein can bind to those of the second fusion protein (throughout document, see particularly p 70, col 1, para 4, Fig. 1).

Regarding present **claim 3**, Crameri et al. teach a second fusion protein comprising a cDNA from a cDNA library (see p 70, col 1, para 4, Fig. 1).

Regarding **claims 4-5**, Crameri et al. teach the M13 pIII phage coat protein (see p 70, col 2, para 2).

Regarding **claim 6**, Crameri et al. teach the first fusion protein with a Jun leucine zipper interaction domain and the second fusion protein with a Fos leucine zipper interaction domain (see p 70, col 2, para 2).

Regarding **claim 7**, Crameri et al. teach wherein the first fusion protein comprises the pelB signal sequence (i.e.: Sec-dependent signal sequence; see p 70, col 1, para 4, col 2, para 2, Fig. 1).

Regarding **claim 9**, Crameri et al. teach covalent linking of the Jun and Fos leucine zippers (i.e.: the first fusion protein is covalently bound to the second fusion protein through the leucine zippers; see p 70, col 1, para 4, Fig. 1).

Although Crameri et al. teach first and second fusion proteins covalently bound, Crameri et al. do not teach a second fusion protein comprising a Tat-dependent translocation sequence.

Regarding present **claims 1 and 8**, Weiner et al. (as evidenced by Wu et al., where the Mtt pathway and the Tat pathway are the same pathway; see abstract, p 319, col 2) teach a Tat-dependent translocation sequence that transports folded proteins through the cytoplasmic membrane (see Weiner et al., col 1, 2, 10, and examples 1-5).

It would have been obvious to one of skill in the art to use the Tat-dependent translocation sequence taught by Weiner et al. in the fusion protein mixture taught by

Crameri et al. One would have been motivated to do so to take advantage of the ability of the Tat pathway to transport folded proteins. One would have had a reasonable expectation for success because Weiner et al. teach that the translocation sequences translocate functional folded proteins through the cell membrane (see col 1, 2, 10, and col 35, para 2 - col 36, para 1). Therefore, the teachings of Crameri et al. and Weiner et al. render the present invention to be *prima facie* obvious.

Claims 1 and 3-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crameri et al. (Display of biologically active proteins on the surface of filamentous phages: a cDNA cloning system for selection of functional gene products linked to the genetic information responsible for their production, 1993, Gene, vol 137, pp 69-75) and Georgiou et al. (US Patent 7,419,783, filed November 5, 2002, with benefit to provisional applications 60/404944, filed August 21, 2002, and 60/337452, filed November 5, 2001).

Regarding present **claim 1**, Crameri et al. teach a) a first fusion protein comprising: i) PIII (i.e.: a protein or protein fragment; see p 70, col 2, para 2), ii) a Jun Leucine zipper interaction domain (see p 70, col 1, para 4, col 2, para 2, and iii) wherein PIII is the phage coat protein comprising the pelB signal sequence (i.e.: a protein translocation sequence which effects that the fusion protein upon expression in a bacterium is translocated through the cytoplasmic membrane in an essentially unfolded state; see p 70, col 1, para 4, col 2, para 2, Fig. 1), and b) a second fusion protein comprising: i) a cDNA from a cDNA library (i.e.: protein or protein fragment), ii) a Fos

Leucine zipper interaction domain (see p 70, col 1, para 4, col 2, para 2), and iii) a pelB signal sequence (i.e.: a protein translocation sequence which effects that the fusion protein upon expression in a bacterium is translocated through the cytoplasmic membrane), wherein the interaction domain of the first fusion protein can bind to those of the second fusion protein (throughout document, see particularly p 70, col 1, para 4, Fig. 1).

Regarding present **claim 3**, Crameri et al. teach a second fusion protein comprising a cDNA from a cDNA library (see p 70, col 1, para 4, Fig. 1).

Regarding **claims 4-5**, Crameri et al. teach the M13 pIII phage coat protein (see p 70, col 2, para 2).

Regarding **claim 6**, Crameri et al. teach the first fusion protein with a Jun leucine zipper interaction domain and the second fusion protein with a Fos leucine zipper interaction domain (see p 70, col 2, para 2).

Regarding **claim 7**, Crameri et al. teach wherein the first fusion protein comprises the pelB signal sequence (i.e.: Sec-dependent signal sequence; see p 70, col 1, para 4, col 2, para 2, Fig. 1).

Regarding **claim 9**, Crameri et al. teach covalent linking of the Jun and Fos leucine zippers (i.e.: the first fusion protein is covalently bound to the second fusion protein through the leucine zippers; see p 70, col 1, para 4, Fig. 1).

Although Crameri et al. teach first and second fusion proteins covalently bound, Crameri et al. do not teach a second fusion protein comprising a Tat-dependent translocation sequence.

Regarding present **claims 1 and 8**, Georgiou et al. teach a Tat-dependent translocation sequence that transports the folded proteins it is fused to through the cytoplasmic membrane (Throughout document, see particularly columns 1,2 and examples 7 and 8).

It would have been obvious to one of skill in the art to use the Tat-dependent translocation sequence taught by Georgiou et al. in the fusion protein mixture taught by Crameri et al. One would have been motivated to do so to take advantage of the ability of the Tat pathway to transport folded proteins. One would have had a reasonable expectation for success because Georgiou et al. teach that the Tat-dependent translocation sequences translocate functional folded proteins through the cell membrane (throughout document, see particularly examples 7 and 8). Therefore, the teachings of Crameri et al. and Georgiou et al. render the present invention to be *prima facie* obvious.

Future Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHANNON JANSSEN whose telephone number is (571)270-1303. The examiner can normally be reached on Generally M-F 9:00AM-6:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Primary Examiner, Art Unit 1639

Shannon L Janssen